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[RUSH] **MESSAGE:** Data cut-off on page 15 of SPEC of 8/24/00.

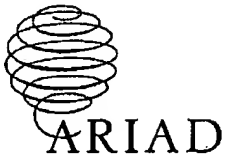
Thank you.

[XRUSH] **RESPONSE:** New page 15 attached

INITIALS: KT

NOTE: This form will be included as part of the official USPTO record, with the Response document coded as XRUSH.

REV 10/04



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Date: August 4, 2005
Pages (with cover sheet): 2

From: Sue Wilson
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Original will follow by:	US Mail	Express Mail	**Will Not Follow**

FACSIMILE MESSAGE

Ref: 09/645,967

ARIAD Ref: 393A US

Attached you will find page 15 of 09/645,967 as originally filed which you requested by phone.

If you need anything further, please don't hesitate to contact me.

Thank you.

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Detailed Description of the Invention

Definitions

The definitions and orienting information below will be helpful for a full understanding of this document.

FRB domains are polypeptide regions (protein "domains"), typically of at least about 89 amino acid residues, which are capable of forming a tripartite complex with an FKBP protein and rapamycin (or a 28-epirapalog of this invention). FRB domains are present in a number of naturally occurring proteins, including FRAP proteins (also referred to in the literature as "RAPT1" or RAFT") from human and other species; yeast proteins including Tor1 and Tor2; and a Candida FRAP homolog. Information concerning the nucleotide sequences, cloning, and other aspects of these proteins is already known in the art, permitting the synthesis or cloning of DNA encoding the desired FRB peptide sequence, e.g., using well known methods and PCR primers based on published sequences.

protein source	reference/sequence accession numbers
human FRAP	Brown et al, 1994, Nature 369, 756-758; GenBank accession # L34075, NCBI Seq ID 508481; Chiu et al, 1994, PNAS USA 91, 12574-12578; Chen et al, 1995, PNAS USA 92, 4947-4951
murine RAPT1	Chiu et al, supra.
yeast Tor1	Helliwell et al, 1994, Mol Cell Biol 5, 105-118; EMBL Accession #X74857, NCBI Seq Id #468738
yeast Tor 2	Kunz et al, 1993, Cell 73, 585-596; EMBL Accession #X71416, NCBI Seq ID 298027
Candida TOR	WO95/33052 (Berlin et al)

FRB domains for use in this invention generally contain at least about 89 - 100 amino acid residues. Fig.2 of Chiu et al, supra, displays a 160-amino acid span of human FRAP, murine FRAP, *S. cerevisiae* TOR1 and *S. cerevisiae* TOR2 encompassing the conserved FRB region. Typically the FRB sequence selected for use in fusion proteins of this invention will span at least the 89-amino acid sequence Glu-39 through Lys/Arg-127, as the sequence is numbered in that figure. For reference, using the numbering of Chen et al or Sabitini et al, the 89-amino acid sequence is numbered Glu-2025 through Lys-2113 in the case of human FRAP, Glu-1965 through Lys-2053 in the case of Tor2, and Glu-1962 through Arg-2050 in the case of Tor1. An FRB domain for use in fusion proteins of this invention will be capable of binding to a complex of an FKBP protein bound to rapamycin or a 28-epirapalog of this invention (as may be determined by any means, direct or indirect, for detecting such binding, including, for example, means for detecting such binding employed in the FRAP/RAFT/RAPT and Tor-related references cited herein). The peptide sequence of such an FRB domain comprises (a) a naturally occurring peptide sequence spanning at least the indicated 89-amino acid region of the proteins noted above or corresponding regions of homologous proteins; (b) a variant of a naturally occurring FRB sequence in which up to about ten (preferably 1-5, more preferably 1-3, and in some embodiments just one) amino acids of the naturally-occurring peptide sequence have

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